REMARKS

I. Status of the Claims. The present Amendment cancels claims 77-80 and 83-86 Claims 14 and 20 have been amended to replace the term "subject" with term "patient" as the last word of each respective claim. Claims 19, 25, 93 and 105 and have been amended to delete the phrase "a bispecific antibody, an artificial antibody." All cancellations and/or amendments to the claims are made without prejudice or disclaimer as to all cancelled subject matter.

By this Amendment, no new matter has been added to the application.

II. Interview Summary. On December 3, 2008, Applicant's representative Mitch Bernstein (Reg. No. 46,550) conducted a telephonic interview with Examiner Emch of the USPTO, during which time the Final Office Action was discussed. No agreement was reached on allowable subject matter. Applicant's representative suggested, however, that the number of outstanding issues would be reduced by amending the claims to delete all subject matter that the Examiner has asserted is not supported by provisional application 60/041,850 (to which the instant application claims the benefit of priority) and thus, according to the Examiner, causes certain claims to not be entitled to the 9 April 1997 filing date of the provisional application. Discussion focused on whether an Amendment that deleted the term " an artificial antibody" from the claims would be entered. The Examiner indicated that he would give full consideration to entry of claims amended to delete "artificial antibody." Applicant's representative wishes to thank Examiner Emch for the courtesies extended during the interview.

It is noted that the present amendment also deletes the term "a bispecific antibody" from the claims, which is believed to comport with discussion during the interview that all subject matter that might raise issues as to entitlement to the priority date of April 9, 1997 for the present claims would be deleted.

III. Request for Entry of Amendment. The present Amendment After Final Rejection complies with the requirements for entry that are set forth in rule 1.116. Claims 77-80 and 83-86 have been cancelled. *See* rule 1.116(b)(1) (cancellation of claims permitted). Claims 19,

25, 93 and 105 have been amended to delete the terms "a bispecific antibody" and "an artificial antibody." As discussed below, in section IV, upon deletion of "bispecific antibody" and "artificial antibody" from the aforementioned claims, these claims and other claims that depend upon them become entitled to the benefit of the priority date of April 9, 1997 (based on the filing date of provisional application 60/041,850), which in turn obviates all prior art rejections. Thus, the amendments deleting "bispecific antibody" and "artificial antibody" put the claims in better form for appeal by materially reducing the issues for appeal. *See* rule 1.116 (b)(2) (amendment putting claims in better form for consideration on appeal may be entered) and MPEP 714.13 section II. (claims removing issues for appeal may be entered). Lastly, none of pending prior art rejections is based on prior art disclosure of either of "a bispecific antibody" or "an artificial antibody." Deletion of these terms from the claims is therefore not believed to raise issues that would require further consideration or search by the Examiner. Claims 14 and 20 have been amended to substitute the term "patient" for "subject." These amendments are not believed to change the scope of the claims and put the claims in better condition for appeal and should thus be entered. In summary, the present Amendment After Final Rejection is believed to comply with the guidelines required for entry that are set out in rule 1.116. Entry of the present Amendment After Final Rejection is respectfully requested.

IV. Priority Date. Each of the subsisting claims is entitled to the benefit of the April 9, 1997 filing date of provisional application 60/041,850. The Examiner's acknowledgement that claims 14, 55, 56, 72 and 75 fully comply with section 112, first paragraph and are thus entitled to the April 9, 1997 of provisional application 60/041,850 is gratefully acknowledged. The Examiner asserts, however, that claims 19, 25, 77-80, 83-86, 93-98 and 105-108 are denied the benefit of the April 9, 1997 priority date because of recitation of "an artificial antibody" in claims 19, 20, 80, 86, 93 and 105 or recitation of particular antibody specificities that are recited in claims 77-79 and 83-85.

The Examiner's failure to accord claims 94, 95, 106 and 108 the filing date of the provisional application for recitation of "an artificial antibody" is believed to be mistaken. Claims

94 and 106 call for "a humanized antibody or fragment thereof" and claims 95 and 108 call for "a chimeric antibody or fragment thereof." Because these claims are not directed to "an artificial antibody," the basis for denying priority is mistaken. Support for claims 94, 95, 106 and 108 is found in provisional application 60/041,850 at, e.g., page 20, lines 15-26, Fig. 3A-3D, and the description of Fig. 3A-3D found at page 12, lines 5-17. Claims 94, 95, 106 and 108 are thus entitled to the April 9, 1997 filing date of provisional application 60/041,850.

With respect to claims 19, 25, 93, 96-98, 105 and 108, claims 19, 25, 93, and 105 have been amended to delete the phrase "an artificial antibody" (as well as the term "a bispecific antibody"). The basis for denying claims 19, 25, 93, 96-98, 105 and 108 the a priority date of April 9, 1997 based on provisional application 60/041,850 is thus believed to have been addressed and overcome.

Claims 77-80 and 83-86 have been cancelled. The failure to accord these claims priority to provisional application 60/041,850 is thus moot.

In summary, all subsisting claims are believed to be entitled to the priority of the April 9, 1997 filing date of provisional application 60/041,850.

V. Claim Rejections. The claim rejections set out in the Final Office Action are summarized and addressed as follows.

(i) Rejections Under 35 U.S.C. §§102 and 103.

Claims 19, 25, 93, 96-98, 105 and 108 have been rejected as allegedly anticipated by Bard et al., *Nature Med.* 6:916-919 (2000). Claims 19, 25, 77, 80, 83, 86, 93-98 and 105-108 have been rejected as allegedly anticipated by Schenk, U.S. Patent No. 6,787,637 ("Schenk").

As set forth above in section IV, the subsisting claims are entitled to a priority date of April 9, 1997. Bard was published in August 2000, i.e., after the priority date of the pending claims. Schenk has an earliest claimed priority date of May 28,1999, i.e., after the priority date of the pending claims. Thus, neither Bard nor Schenk is prior art to the pending claims. Accordingly, all rejections under section §102 should be withdrawn.

(i) Rejection Under 35 U.S.C. § 103.

Claims 77-80 and 83-86 have been rejected as allegedly obvious over Schenk in view of Saido et al., *Neurosci. Lett.* 215:173-176 (1996) and Harigaya et al., *Biochem. Biophys. Res. Comm.* 276:422-427 (2000). In response, without conceding the merits of the rejection, claims 77-80 and 83-86 have been cancelled. The instant rejection is thus moot.

(iii) Rejections Under 35 U.S.C. § 112, second paragraph

Claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80, 83-86, 93-98, 105-108 are rejected as indefinite for allegedly being incomplete for omitting essential steps that amount to a gap between the steps. The Examiner states that the omitted step is the step of delivery of a free-end specific anti-Aβ antibody to a patient. The instant rejection should be withdrawn because the Examiner has failed to provide either of a legal or factual basis for finding the claims indefinite.

The instant rejection is first not believed to be well taken because the stated basis for the rejection— "as being incomplete for omitting essential steps, such omission amounting to a gap between the steps" — is not a ground for rejection under section 112, second paragraph. Claims are definite if "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986) (citations omitted). The "lack of an essential step" is not a basis for rejecting the claims under section 112, second paragraph.

Moreover, the factual basis set forth for the rejection is mistaken. The Examiner is first mistaken to assert the claimed methods lack an essential step. Claims 14, 19, 55 and 72 are directed to a method for inhibiting accumulation of Aβ in the brain of an Alzheimer's disease patient comprising the step of "contacting in vivo soluble amyloid β peptide in the cerebrospinal fluid of said patient with an exogenous free-end specific antibody" with the stated specificities, "to inhibit the accumulation of said amyloid β peptide in the brain of said patient." Claims 20, 25, 56 and 72 and are directed to a method for inhibiting the neurotoxicity of Aβ in the brain of an Alzheimer's disease patient comprising the step of "contacting in vivo soluble amyloid β peptide in

the cerebrospinal fluid of said patient with an exogenous free-end specific antibody" with the stated specificities, "to inhibit the neurotoxicity of amyloid β peptide in said patient." As set forth in the Declaration of Dr. Howard J. Federoff Under 37 C.F.R. §1.132 that was submitted August 29, 2007 ("First Federoff Declaration"), upon contacting soluble Aβ in the CSF, exogenous free-end specific antibody will bind to Aβ and inhibit the accumulation and neurotoxicity of Aβ in the brain. *See* First Federoff Declaration at paragraph 15. No step other than contacting Aβ in the CSF is required. In short, only a single step of contacting Aβ in the CSF with a free end-specific antibody (which step is present in each of claims 14, 19, 20, 25, 56, 55 or 72) is sufficient to inhibit the accumulation or neurotoxicity of Aβ in the brain of an Alzheimer's patient. Thus none of claims 14, 19, 20, 25, 56, 55 or 72 lacks an essential step. *See also In re Miller,* 441 F.2d 689, 693 (CCPA 1971) (Breadth of a claim is not to be equated with indefiniteness).

With respect to claims 93-98 and 105-108, these claims are directed to methods of "obtaining an amyloid β-peptide-antibody complex comprising forming a composition essentially of" an end-specific antibody of the given specificities, CSF and Aβ. *See* claims 93 and 105. The Examiner has said the failure to include an essential step extends to claims 93-98 and 105-108 without providing any guidance as to what the missing step might be. Forming a composition essentially of an end-specific antibody, CSF and Aβ, as called for in claims 93 and 105, will lead to formation of complexes of an amyloid β-peptide-antibody complex. No additional steps are required. Claims 93-98 and 105-108 thus do not lack an essential step.

The Examiner asserts that even if the specification does not teach that administration is an essential step (which, as set out above the specification does not teach) the claims are nonetheless indefinite because without an administration step it is unclear how the exogenous antibodies would be present in vivo and it is open as to where the contacting step occurs. The Examiner assertions are believed to be mistaken, on both counts.

The Examiner is first mistaken to conclude that it is unclear how exogenous antibodies would be present in vivo. As set forth in Applicant's prior response of May 19, 2008, the

specification includes extensive guidance concerning how exogenous antibodies may be administered, e.g., by intravenous administration or by expression of antibody genes in the CNS. *See* specification at pages 11-13. The present application and the provisional application on which it is based disclose that antibodies contact amyloid-β protein after being secreted into the CSF from neuronal cells or after they cross the blood brain barrier. Moreover, the Declaration of Dr. Kenneth L. Rock Under 37 C.F.R. §1.132 that was submitted August 29, 2007 ("First Rock Declaration") states, "[I]t is my opinion that as of the filing date of the provisional application, upon reading the specification, one of ordinary skill in the art would have immediately appreciated that treatment of Alzheimer's disease by contacting Aβ in the CSF with a free-end specific antibody could be effected by directly administering such antibodies to a patient." First Rock Declaration at paragraph 15. Thus, contrary to the Examiner's assertions, the application sets forth how exogenous antibodies may be present in vivo and, moreover, the ordinarily skilled worker "would have immediately appreciated" how exogenous antibodies could be contacted with Aβ in the CSF. The Examiner is thus mistaken to conclude that it is unclear how exogenous antibodies would be present in vivo.

The Examiner is also mistaken to conclude where the "contacting" step takes place. Claims 14, 19, 20, 25, 55, 56 and 72 are directed to methods that call for "contacting in vivo soluble amyloid β peptide in the cerebrospinal fluid of said patient." *See* claims 14 and 20. These claims thus state explicitly that the "contacting" step takes place in the CSF of a patient. Moreover, to the extent that further interpretation of the claims is required (which is not believed to be the case), as discussed above, the specification discloses that antibodies contact amyloid-β protein after being secreted into the CSF from neuronal cells or after they cross the blood brain barrier (into the CSF). There is thus no ambiguity that the "contacting" step called for in claims 14, 19, 20, 25, 55, 56 and 72 occurs in the CSF of a patient.[1]

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[1] Claims 93-98 and 105-108, do not include a step that calls for "contacting." The objection based on the indefiniteness of a "contacting" step thus does not apply to these claims.

Other points raised by the Examiner in setting forth the instant rejection are addressed as follows.

The Examiner mistakenly implies that Applicant's reference to the specification reads limitations from the specification into the claims. The Applicant, does not seek to read limitations from the specification into the claims. The Applicant has simply pointed out that the claims are definite because, when read in light of the specification, one of ordinary skill in the art would understand that: (1) when the claims call for a method "comprising contacting in vivo soluble amyloid β peptide in the cerebrospinal fluid of said patient with an exogenous free-end specific antibody," the exogenous antibody may be administered in different ways; (2) the "contacting step takes place in the CSF of the patient;" and (3) methods of inhibiting accumulation or inhibiting neurotoxicity of Aβ in the brain require only the single "contacting" step that is called for in the claims.

It is always permissible to look to the specification to ascertain whether the claims are definite-- "[T]he definiteness of the language employed must be analyzed-not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore,* 439 F.2d 1232, 1235 (CCPA 1971). *See also Orthokinetics, Inc. v. Safety Travel Chairs, Inc.,* 806 F.2d 1565, 1576 (Fed. Cir. 1986) (Test for definiteness is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification."); *Miles Laboratories, Inc. v. Shandon, Inc.,* 997 F.2d 870, 875 (Fed. Cir. 1993) ("The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification."); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1385 (Fed. Cir. 1986) (Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits)." Thus, it is not improper for Applicant to look to the specification to demonstrate the instant claims are definite.

In summary, the subsisting claims satisfy both the legal and policy standards for compliance with 112, second paragraph. When "read in light of the specification" the instant claims "reasonably apprise those skilled in the art both of the utilization and scope of the invention." Moreover, notwithstanding the alleged indefiniteness of the claims, during the course of prosecution of this application in the USPTO, three different examiners have found the claims sufficiently definite to carry out meaningful examination and issue six substantive Official Actions. Thus, the claims are apparently sufficiently definite to "facilitate[] the examination of applications by the Patent and Trademark Office." In short, the scope of the claims is sufficiently clear, so the public is informed of the claim boundaries to enable assessment of activities that would constitute infringement and the Patent Office can carry out examination of the application. The pending claims comply with the strictures of section 112, second paragraph. Reconsideration of this application and withdrawal of the indefiniteness rejection is respectfully requested.

VI. Conclusion. In view of the above amendments and remarks, the pending application is believed to be in condition for allowance, which is earnestly solicited.

Dated: December 11, 2008

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